CLAIMS

What is claimed is:

1. A method for treating or preventing diabetes in a mammalian subject, comprising:

administering a therapeutically effective amount of a gallotannin composition to a subject in need of the same,

wherein said gallotannin composition comprises one or more hydrolysable gallotannins selected from the group consisting of 1,2,3,4-tetra-O-galloyl-α-D-glucose, 1,2,3,6-tetra-O-galloyl-α-D-glucose, 1,3,4,6-tetra-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,2,3,4,6-hexa-galloyl-α-D-glucose, 1,2,3,4,6-hexa-O-galloyl-β-D-glucose, 1,2,3,4,6-hepta-O-galloyl-α-D-glucose, 1,2,3,4,6-hepta-O-galloyl-β-D-glucose, 1,2,3,4,6-octa-O-galloyl-α-D-glucose, 1,2,3,4,6-octa-O-galloyl-β-D-glucose, 1,2,3,4,6-nona-O-galloyl-α-D-glucose, 1,2,3,4,6-nona-O-galloyl-β-D-glucose, 1,2,3,4,6-deca-O-galloyl-α-D-glucose, and 1,2,3,4,6-deca-O-galloyl-β-D-glucose, or a salt thereof, and

wherein said gallotannin composition comprises less than 5% by dry weight of one or more of the following compounds: mono-O-galloyl-β-D-glucose, di-O-galloyl-β-D-glucose, tri-O-galloyl-β-D-glucose, tetra-O-galloyl-β-D-glucose, unadeca-O-galloyl-β-D-glucose, dodeca-O-galloyl-β-D-glucose or mixtures thereof.

2. The method of claim 1 wherein said gallotannin composition comprises at least 50% by dry weight of 1,2,3,4,6-penta-O-galloyl-α-D-glucose or 1,2,3,4,6-penta-O-galloyl-β-D-glucose or a combination of 1,2,3,4,6-penta-O-galloyl-α-D-glucose and 1,2,3,4,6-penta-O-galloyl-β-D- glucose.

3. The method of claim 1 wherein said gallotannin composition comprises at least 50% by dry weight of 1,2,3,4,6-penta-O-galloyl-α-D-glucose.

4. The method of claim 1 wherein said gallotannin composition comprises at least 50% by dry weight of 1,2,3,4,6-penta-O-galloyl-β-D-glucose.

5. The method of claim 1 wherein said gallotannin composition is administered to the subject orally or by injection.

6. The method of claim 1 further comprising the step of administering insulin to the subject.

7. A method for treating or preventing diabetes in a subject, comprising:

administering a gallotannin variant composition to the subject,

wherein said gallotannin variant composition comprises one or more gallotannin variant compounds or a salt thereof, wherein each of said gallotannin variant compounds has the following structure:

$$R\text{-}X\text{-}A(_n)\text{-}X\text{-}A(_q)\text{-}X\text{-}A(_z),$$

wherein R is selected from the group consisting of D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, D-glucitol,

X is an ester or ether linkage,

A is a trihydroxybenzoic acid selected from the group consisting of 3,4,5-trihydroxybenzoic acid, 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid,

n is 5, q is 0, 1, 2, 3, 4, or 5, and z is 0 when R is D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose;

n is 4, q is 0, 1,2, 3, or 4, and z is 0, 1, or 2 when R is α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose;

n is 6, q is 0, 1, 2, 3, 4, 5, or 6, and z is 0 when R is D-Glucitol or *myo*-Inositol, and

n is 8, q is 0, 1, 2, 3, 4, 5, 6, 7, or 8, and z is 0 when R is D-Trehalose, D-Maltose, D- or Cellobiose.

8. The method of claim 7 wherein X is an ether linkage.

9. The method of claim 7 wherein R is L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, or D-glucitol.

10. The method of claim 4 wherein A is a trihydroxybenzoic acid selected from the group consisting of 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid.

11. The method of claim 4 wherein each of said gallotannin variant compounds has a structure other than the structure tetra-O-galloyl-β-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,2,3,4,6-hexa-O-galloyl-β-D-glucose, 1,2,3,4,6-hepta-O-galloyl-β-D-glucose, 1,2,3,4,6-octa-O-galloyl-β-D-glucose, 1,2,3,4,6-nona-O-galloyl-β-D-glucose, and 1,2,3,4,6-deca-O-galloyl-β-D-glucose.

12. A method of reducing elevated blood glucose levels in a subject in need thereof without causing hypoglycemia in the subject, comprising:

administering one or both of the following compositions (a) and (b) to the subject,

(a) a gallotannin composition which comprises one or more hydrolysable gallotannins selected from the group consisting of wherein said gallotannin composition comprises one or more hydrolysable gallotannins selected from the group consisting of 1,2,3,4-tetra-O-galloyl-α-D-glucose, 1,2,3,6-tetra-O-galloyl-α-D-glucose, 1,3,4,6-tetra-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-

glucose, 1,2,3,4,6-hexa-galloyl-α-D-glucose, 1,2,3,4,6-hexa-O-galloyl-β-D-glucose, 1,2,3,4,6-hepta-O-galloyl-α-D-glucose, 1,2,3,4,6-hepta-O-galloyl-β-D-glucose, 1,2,3,4,6-octa-O-galloyl-α-D-glucose, 1,2,3,4,6-octa-O-galloyl-β-D-glucose, 1,2,3,4,6-nona-O-galloyl-α-D-glucose, 1,2,3,4,6-nona-O-galloyl-β-D-glucose, 1,2,3,4,6-deca-O-galloyl-α-D-glucose, and 1,2,3,4,6-deca-O-galloyl-β-D-glucose, or a pharmaceutically acceptable salt thereof, and

wherein said gallotannin composition comprises less than 5% by dry weight of one or more of the following compounds: mono-O-galloyl-β-D-glucose, di-O-galloyl-β-D-glucose, tri-O-galloyl-β-D-glucose, tetra-O-galloyl-β-D-glucose, unadeca-O-galloyl-β-D-glucose, dodeca-O-galloyl-β-D-glucose or mixtures thereof;

(b) a gallotannin variant composition which comprises one or more compounds having the following structure, or a pharmaceutically acceptable salt thereof:

$$R\text{-}X\text{-}A(_n)\text{-}X\text{-}A(_q)\text{-}X\text{-}A(_z),$$

wherein R is selected from the group consisting of D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, D-glucitol,

X is an ester or ether linkage,

A is a trihydroxybenzoic acid selected from the group consisting of 3,4,5-trihydroxybenzoic acid, 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid,

n is 5, q is 0, 1, 2, 3, 4, or 5, and z is 0 when R is D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose;

n is 4, q is 0, 1,2, 3, or 4, and z is 0, 1, or 2 when R is α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose;

n is 6, q is 0, 1, 2, 3, 4, 5, or 6, and z is 0 when R is D-Glucitol or *myo*-Inositol, and

n is 8, q is 0, 1, 2, 3, 4, 5, 6, 7, or 8, and z is 0 when R is D-Trehalose, D-Maltose, or D- Cellobiose.

13. A method of treating a subject exhibiting one or more of obesity, type II diabetes, glucose intolerance, insulin resistance, hyperglycemia, or hyperinsulinemia comprising

administering a gallotannin composition to the subject,

wherein said gallotannin composition comprises one or more hydrolysable gallotannins selected from the group consisting of wherein said gallotannin composition comprises one or more hydrolysable gallotannins selected from the group consisting of 1,2,3,4-tetra-O-galloyl-α-D-glucose, 1,2,3,6-tetra-O-galloyl-α-D-glucose, 1,3,4,6-tetra-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,2,3,4,6-hexa-galloyl-α-D-glucose, 1,2,3,4,6-hexa-O-galloyl-β-D-glucose, 1,2,3,4,6-hepta-O-galloyl-α-D-glucose, 1,2,3,4,6-hepta-O-galloyl-β-D-glucose, 1,2,3,4,6-octa-O-galloyl-α-D-glucose, 1,2,3,4,6-octa-O-galloyl-β-D-glucose, 1,2,3,4,6-nona-O-galloyl-α-D-glucose, 1,2,3,4,6-nona-O-galloyl-β-D-glucose, 1,2,3,4,6-deca-O-galloyl-α-D-glucose, and 1,2,3,4,6-deca-O-galloyl-β-D-glucose, or a salt theeof, and

wherein said gallotannin composition comprises less than 5% by dry weight of one or more of the following compounds: mono-O-galloyl-β-D-glucose, di-O-galloyl-β-D-glucose, tri-O-galloyl-β-D-glucose, tetra-O-galloyl-β-D-glucose, unadeca-O-galloyl-β-D-glucose, dodeca-O-galloyl-β-D-glucose or mixtures thereof.

14. The method of claim 13 wherein administration of said gallotannin composition inhibits differentiation of preadipocytes to adipocytes in the subject.

15. The method of claim 13 wherein said gallotannin composition is administered to the subject orally or by injection.

16. A method of inhibiting differentiation of preadipocytes to adipocytes in vitro or in vivo, comprising:

contacting the preadipocytes with a gallotannin composition,

wherein said gallotannin composition comprises one or more hydrolysable gallotannins selected from the group consisting of 1,2,3,4-tetra-O-galloyl-α-D-glucose, 1,2,3,6-tetra-O-galloyl-α-D-glucose, 1,3,4,6-tetra-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-α-D-glucose, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,2,3,4,6-hexa-galloyl-α-D-glucose, 1,2,3,4,6-hexa-O-galloyl-β-D-glucose, 1,2,3,4,6-hepta-O-galloyl-α-D-glucose, 1,2,3,4,6-hepta-O-galloyl-β-D-glucose, 1,2,3,4,6-octa-O-galloyl-α-D-glucose, 1,2,3,4,6-octa-O-galloyl-β-D-glucose, 1,2,3,4,6-nona-O-galloyl-α-D-glucose, 1,2,3,4,6-nona-O-galloyl-β-D-glucose, 1,2,3,4,6-deca-O-galloyl-α-D-glucose, and 1,2,3,4,6-deca-O-galloyl-β-D-glucose, or salts thereof.

17. The method of claim 16 wherein said gallotannin composition comprises less than 5% by dry weight of one or more of the following compounds: mono-O-galloyl-β-D-glucose, di-O-galloyl-β-D-glucose, tri-O-galloyl-β-D-glucose, tetra-O-galloyl-β-D-glucose, unadeca-O-galloyl-β-D-glucose, dodeca-O-galloyl-β-D-glucose or mixtures thereof.

18. The method of claim 16 wherein said gallotannin composition comprises at least 50% by dry weight of 1,2,3,4,6-penta-O-galloyl-α-D-glucose or 1,2,3,4,6-penta-O-galloyl-β-D-glucose or a combination of 1,2,3,4,6-penta-O-galloyl-α-D-glucose and 1,2,3,4,6-penta-O-galloyl-β-D- glucose.

19. The method of claim 16 wherein said gallotannin composition comprises at least 50% by dry weight of 1,2,3,4,6-penta-O-galloyl-β-D-glucose.

20. A method of inhibiting differentiation of preadipocytes to adipocytes in vitro or in vivo, comprising

contacting the preadipocytes with a composition comprising one or more compounds having the following structure, salts thereof:

$$R\text{-}X\text{-}A(_n)\text{-}X\text{-}A(_q)\text{-}X\text{-}A(_z),$$

wherein R is selected from the group consisting of D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, D-glucitol,

X is an ester or ether linkage,

A is a trihydroxybenzoic acid selected from the group consisting of 3,4,5-trihydroxybenzoic acid, 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid,

n is 5, q is 0, 1, 2, 3, 4, or 5, and z is 0 when R is D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose;

n is 4, q is 0, 1,2, 3, or 4, and z is 0, 1, or 2 when R is α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose;

n is 6, q is 0, 1, 2, 3, 4, 5, or 6, and z is 0 when R is D-Glucitol or *myo*-Inositol, and

n is 8, q is 0, 1, 2, 3, 4, 5, 6, 7, or 8, and z is 0 when R is D-Trehalose, D-Maltose, or D-Cellobiose.

21. A gallotannin variant composition, comprising one or more gallotannin variant compounds, or a pharmaceutically acceptable salt thereof, wherein each of said gallotanin variant compounds have the following structure:

$$R\text{-}X\text{-}A(_n)\text{-}X\text{-}A(_q)\text{-}X\text{-}A(_z),$$

wherein R is selected from the group consisting of D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, D-glucitol,

X is an ester or ether linkage,

A is a trihydroxybenzoic acid selected from the group consisting of 3,4,5-trihydroxybenzoic acid, 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid,

n is 5, q is 0, 1, 2, 3, 4, or 5, and z is 0 when R is D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose;

n is 4, q is 0, 1,2, 3, or 4, and z is 0, 1, or 2 when R is α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose;

n is 6, q is 0, 1, 2, 3, 4, 5, or 6, and z is 0 when R is D-Glucitol or *myo*-Inositol, and

n is 8, q is 0, 1, 2, 3, 4, 5, 6, 7, or 8, and z is 0 when R is D-Trehalose, D-Maltose, or D-Cellobiose,

and

wherein each of said gallotannin variant compounds is not a beta anomeric form of tetra-O-galloyl-D-glucose, penta-O-galloyl-D-glucose, hexa-galloyl-α-D-glucose, hepta-O-galloyl-D-glucose, octa-O-galloyl-D-glucose, nona-O-galloyl-D-glucose, or deca-O-galloyl-D-glucose.

22. The composition of claim 21 wherein the composition comprises Pentakis-O-(3,4-dihydroxybenzoyl)-β-D-glucopyranose, or tetrakis-O-(3,4,5-trihydroxybenzoyl)-α-D-xylopyranose.

23. A compound for treating diabetes insulin resistance, impaired glucose tolerance, hyperglycemia, hyperinsulinemia or obesity in a subject, said compound having the following formula:

$$R\text{-}X\text{-}A(_n)\text{-}X\text{-}A(_q)\text{-}X\text{-}A(_z),$$

wherein R is selected from the group consisting of D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose, α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose, D-Trehalose, D-Maltose, D-Cellobiose, *myo*-Inositol, D-glucitol,

X is an ester or ether linkage,

A is a trihydroxybenzoic acid selected from the group consisting of 3,4,5-trihydroxybenzoic acid, 2,3,4-trihydroxybenzoic acid 2,4,6-trihydroxybenzoic acid, or a dihydroxybenzoic acid selected from the group consisting of 2,3-dihydroxybenzoic acid, 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, or a monohydroxybenzoic acids selected from the group consisting of 3-hydroxybenzoic acid and 4-hydroxybenzoic acid,

n is 5, q is 0, 1, 2, 3, 4, or 5, and z is 0 when R is D-Glucose, L-Glucose, D-Mannose, L-Mannose, D-Galactose, L- Galactose, D-Allose, L-Allose, D-Altrose, L-Altrose D-Gulose, L-Gulose, D-Idose, L-Idose, D-Talose, L, Talose, D-Fructose, L-Fructose;

n is 4, q is 0, 1,2, 3, or 4, and z is 0, 1, or 2 when R is α-D-Xylose, α-D Lyxose, β-D Lyxose, α-D Arabinose, β-D Arabinose, α-D Ribose, β-D Ribose;

n is 6, q is 0, 1, 2, 3, 4, 5, or 6, and z is 0 when R is D-Glucitol or *myo*-Inositol, and

n is 8, q is 0, 1, 2, 3, 4, 5, 6, 7, or 8, and z is 0 when R is D-Trehalose, D-Maltose, or D- Cellobiose,

or a pharmaceutically acceptable salt of said compound.

24. A pharmaceutical composition for treating insulin resistance, impaired glucose tolerance, hyperglycemia, hyperinsulinemia or obesity in a subject, said pharmaceutical composition comprising an effective amount of the compound of claim 23 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.